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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,430	02/17/2000	Lawrence R. Green	15542-002310	6441

7590 04/09/2004

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/506,430	GREEN ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003 and 16 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-72* is/are pending in the application.

4a) Of the above claim(s) *36-38 and 64-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-35,39-63 and 67-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed (12/16/03), claims 18, 19, 23, 24, 40, 41 have been amended, and claims 46-72 added. Claims 18-72 are now pending. Claims 36-38 and 64-66 are withdrawn from consideration. Claims 18-35, 39-63, 67-72 are examined in this Office action.

Applicants' arguments filed 10/2/03 have been considered and found persuasive in part. The rejection of claims 18, 19, 21, 22, 28-35 over Haber in view of Rogers is withdrawn. However, this rejection is applicable to (newly added) claim 72.

✧

Claims 18, 45 and 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,902,790 Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 1 of '790 is drawn to a method of inhibiting neovascularization by administering the dipeptide Glu-Trp. Based on this embodiment alone, claims 18, 45 and 48 are rendered obvious. In addition, claim 1 of the patent is drawn to a "cyclic form" of the dipeptide. One interpretation of this would be a diketopiperazine obtained by bonding the alpha-amino group of Glu to the carboxyl group of Trp. Instant claim 18 could be interpreted to encompass this, since both R' and R" can be "absent". Finally, claim 1 of the patent is also drawn to a method of inhibiting neovascularization by administering an oligomer of the dipeptide Glu-Trp. Regardless of the size of the

oligomer, there will always be a Glu-Trp at the C-terminus, and a Glu-Trp at the N-terminus; accordingly claims 18 and 48 are rendered obvious in the case of oligomers.

> The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application . See 37 CFR 1.78(d)

✧

Claims 18-35, 39-63, 67-72 are rejected under 35 U.S.C. . 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 18 provides a definition of R". Within that definition, the possibility of R" (taken together with the carbonyl of tryptophan) to represent an amide is not included. At the same time, claim 18 recites (within the last five lines of text) that R' and R" are not both amide. This particular phrase appears to be superfluous, however, since R" cannot be amide under any circumstances anyway.

- Applicants are requested to confirm that in claim 22, the term "tosulate" is indeed intended, and not *tosylate*.

- Claim 72 recites that the molecular weight of the compound is "about" 1000 D, whereas claim 48, upon which claim 72 depends, does not permit the molecular weight to be as high as 1000 Daltons. Thus, even for the case in which the MW of the compound is exactly equal to 1000 Daltons, claim 72 is not properly subgeneric to claim 48, and certainly for the case when the MW of the compound is above 1000 D (as permitted by claim 72), the dependence of claim 72 on claim 48 is not proper. The same issue applies in the case of claim 46 *versus* claim 18.

✧

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 72 is rejected under 35 U.S.C. §103 as being unpatentable over Haber [*Prog. Biochem. Pharmacol.* (1976), **12** (Drugs Affecting Renin-Angiotensin- Aldosterone Syst., Proc. Kanematsu Conf. Kidney, 5th), 16-32] in view of Rodgers (USP 5,716,935).

As indicated previously, Haber discloses (e.g., page 17) that the peptide EWPRFQIPP inhibits the enzyme ACE. Haver does not disclose that inhibitors of ACE are also effective to inhibit neovascularization or angiogenesis. Rodgers discloses (col 3, line 5-10) that angiotensin stimulates neovascularization and angiogenesis. Rodgers does not disclose any of the peptides that are encompassed by the instant claims.

The response filed 10/2/03 does not specifically traverse this rejection, other than to assert

that the claim is not rendered obvious by the references. However, the rejection is maintained, since the molecular weight of the peptide is "about" 1000 Daltons, and no explanation is provided as to why the rejection might not be justified.

✧

Claim 72 is rejected under 35 U.S.C. §103 as being unpatentable over Haber [*Prog. Biochem. Pharmacol.* (1976), **12** (Drugs Affecting Renin-Angiotensin- Aldosterone Syst., Proc. Kanematsu Conf. Kidney, 5th), 16-32] in view of Rodgers (USP 5,716,935) further in view of Folkman (*J Natl Cancer Inst* **82**, 4-6, 1990).

The teachings of Haber and of Rodgers were indicated previously. Neither reference discloses that inhibition of neovascularization is "desirable". Folkman discloses that inhibition of neovascularization is "desirable". Folkman does not disclose any of the compounds underlying the instant method claims.

The response filed 10/2/03 does not specifically traverse this rejection, other than to assert that the claim is not rendered obvious by the references. However, the rejection is maintained, since the molecular weight of the peptide is "about" 1000 Daltons, and no explanation is provided as to why the rejection might not be justified.

✧

Claims 18, 39, 47, 72 are rejected under 35 U.S.C. 103 as being unpatentable over Washino (JP 4-279597) in view of Fernandez, L. A. (*Journal of laboratory and*

Clinical Medicine **105** (2) 141-5, 1985) or Le Noble F. A. (*European Journal of Pharmacology* **195** (2) 305-6, 1991).

Washino discloses that the following peptide, designated "RJP8", inhibits angiotensin converting enzyme:

SLPKLHEW

Washino does not disclose that angiotensin stimulates neovascularization or angiogenesis. Fernandez discloses that angiotensin stimulates neovascularization. Similarly, Le Noble discloses that angiotensin stimulates angiogenesis. Neither Fernandez nor Le Noble discloses that a peptide containing the dipeptide subsequence Glu-Trp will inhibit formation of angiotensin.

This peptide is encompassed by the claims when variable R' represents amide. In accordance with the foregoing, it would have been obvious to one of ordinary skill that the peptide of Washino will inhibit formation of angiotensin, and thus inhibit neovascularization and angiogenesis.

Thus, the claims are rendered obvious.

✧

Applicants are advised that the first page of the specification will be amended to recite the continuity status as follows:

> This application is a continuation of application 09/260190, filed 3/1/99, now US Patent 6,096,713. Application 09/260190 is a continuation of application 08/614764, filed 3/13/96, now US Patent 5,902,790. Application 08/614764 is a continuation of

application 08/538701, filed 10/3/95, now abandoned. Application 08/538701 is a C.I.P. of application 08/278463, filed 7/21/94, now abandoned. Application 08/278463 is a C.I.P. of 08/401653 filed 3/9/95, now abandoned, and a C.I.P. of 08/257495 filed 6/7/94, now abandoned, and a C.I.P. of 08/370838 filed 1/10/95, now abandoned, and a C.I.P. of 08/075842 filed 6/10/93, now abandoned. Application 08/075842 is a continuation of 07/678129 filed 4/1/91, now abandoned. Application 08/257495 is a continuation of 07/783518, filed 10/28/91, now abandoned, which is a continuation in part of 07/678129, which is a continuation in part of 07/415283, filed 8/30/89, now abandoned.

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton 4/2/04

CHRISTOPHER S. F. LOW
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